

ABSTRACT OF THE DISCLOSURE

A novel gene therapy for cancer has been discovered, which unlike most prior approaches, does not require specific knowledge of the cancer cells, but instead targets a general characteristic that distinguishes cancer cells from normal cells, i.e., elevated eIF4E expression. The expression of a toxin or conditional toxin such as HTK is translationally repressed in normal cells by placing a complex 5' UTR in front of its reading frame. In prototype experiments, this HTK mRNA, a transcriptional product of the BK-UTK vector, was translationally regulated so as to largely inhibit its production in normal murine and human cells, while cancer cells efficiently translated the protein, which resulted in increased sensitivity to GCV. Synthesis of the HTK protein from the BK-UTK vector (containing the 5' UTR of Fibroblast growth factor - 2 ("FGF-2")) readily occurred in a panel of murine and human breast carcinoma lines, but not in normal cell lines. Subcutaneous tumors and experimental lung metastases of the breast carcinoma line MM2MT in BALB/c mice were greatly reduced by transfection with the BK-UTK vector, followed by GCV administration. Both the BK-UTK and the BK-TK (control) vectors were effective in reducing lung metastasis following systemic delivery of the vectors and subsequent GCV administration. However, the BK-TK vector was highly toxic to mice while little to no toxicity was seen in mice treated with the BK-UTK vector.